Observations on Reflex Responses to Rhythmical Stimulation in the Frog.

By Kanshi Sassa, M.D., Tokio.

(Communicated by Prof. C. S. Sherrington, Pres. R.S. Received July 1, 1921.)

(From the Physiological Laboratory, Oxford.)

The primary object of this investigation was the study of the relation between the frequency and intensity of stimulation, and the resulting reflex reactions. I first studied the effect of alteration of frequency at a given intensity of stimulation and found that under these conditions the frequency has an optimal value. With moderate and rapid frequency stimuli there is also an optimal intensity value, though with those of low frequency this is not the case.

It was also hoped that some light might be thrown on the mechanism of the spinal reflex centre by the comparison of the isometrically recorded reflex tetanus, with the tetanus obtained directly by stimulation of the efferent nerve at varying intensity and frequency of stimulation. In particular, an attempt was made to settle the question as to whether stimulation of a nerve can set into action the whole of the reflex centre to which it is afferent. Camis (4) concluded that the cells of a spinal motor centre can be regarded from a functional point of view, as divided into several independent groups, though this division is not absolute. On the other hand, Dreyer and Sherrington's (5) observations point rather to the physiological unity of the spinal motor centre; since they showed that the maximal mechanical power of tetanic contraction, obtainable from a muscle under spinal reflex action, is sometimes as great as that which can be evoked from it by direct faradisation of the motor nerve itself.

Method.—The semitendinosus reflex preparation of the spinal frog was used in these experiments. The femoral vessels were ligatured in the middle of the thigh so as to diminish loss of blood due to the operation. An afferent nerve, the ipsilateral tibial, peroneal or sciatic nerve or sometimes one of their small branches was employed. When reflex and direct tetanus were compared, the roots of the sciatic nerve were previously exposed by removing the musculature lateral to the urostyle.

To record the muscular contraction, the lower portion of the semitendinosus was isolated from the surrounding muscles, its tendon being fixed to the short arm of a spring myograph. All the tendons of flexors and adductors inserted around the knee-joint were detached, and sometimes the leg was disarticulated

at this joint. The pelvis and femur of the frog was firmly fixed by pins to a cork-plate so that the movement of other muscles of the body might not add to that of the semitendinosus. The whole preparation was enclosed in a moist chamber.

The stimulating apparatus was an inductorium fed by two Daniell's cells. To vary the rate of stimulation the "double wire torsion key" devised by Sherrington* was used. The range of alteration of vibration-frequency of the instrument was between 15 and 88 per second. Throughout the experiments only break-shocks were employed. Care was taken that the cathode of the electrodes was proximal to the anode on the afferent nerve for a reflex, and distal on the motor nerve for a direct stimulation. The frogs were kept over-night in the laboratory before being used for experiment; and the time which elapsed between the decapitation and the commencement of the experiment was usually an hour.

I. *The Influence of Stimulation-frequency upon the Reflex Reaction.*

The summation of stimuli in the reflex centre causes increase in the resulting reflex with increase in the rapidity of the sequence of excitation. Stirling (16) pointed out that when a reflex movement is produced in the frog by stimulating a skin point by successive stimuli—the greater the interval between them the higher is the intensity of the individual stimuli necessary to produce the reflex result, and that increase in frequency is more effective than increase in intensity. In the reflex excitation of automatic centres—for example the vasomotor centre—the reflex effect increases with increase in the frequency of stimulation up to the rate of 20–25 per second (11). Matthæi (14) has recently found that the effective minimal number of stimuli, which just produces a reflex reaction, increases in the majority of cases with the frequency of stimulation, occasionally diminishes at first, then reaches an optimum (frequency of 6–21 per second), and finally increases with the stimulation-frequency. In recording my experimental results I will first present the evidence for an optimal frequency of stimulation, by which is meant the rate of stimulation at any given intensity, which produces the most powerful reflex contraction.

1. *The Optimal Frequency-rate of Stimulation.*—In order to determine this, an afferent nerve was stimulated at fixed intensity but at different frequency-rates, and the series of reflex contractions of the semitendinosus thus evoked was recorded isometrically. The intensity of stimulation selected was usually the optimal for a moderately rapid frequency (see later). The lowest rate of excitation was applied for a time sufficiently long to allow the production of

* A description of this key will appear shortly.

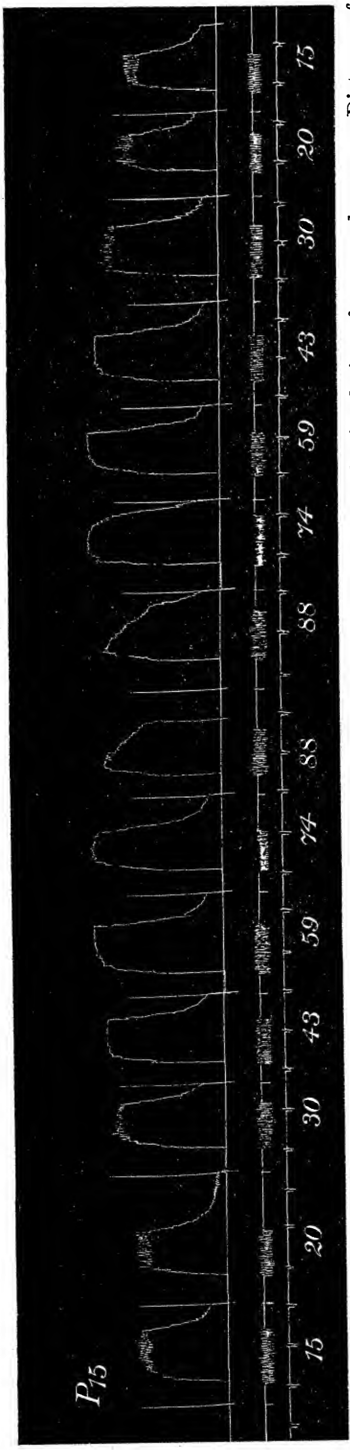

Fig. 1.—Semitendinosus reflex-preparation of spinal frog. Responses at varying frequency of stimulation of peroneal nerve. Distance of coils 15 cm. Threshold value for stimulus, 21 cm. Number of stimuli per second below each response. Time in seconds.

the full contraction it could produce; then, after an interval of about two minutes a somewhat greater rate of stimulation was tried. In this way a series of reflex myograms was obtained at progressively increasing rates, until the maximal frequency which the key could give was reached. This procedure was again repeated in the reverse direction, *i.e.*, progressively decreasing the stimulation-frequency to the initial rate.

The threshold value of faradic stimuli which evoked a reflex response in good preparations was given by a distance between the coils of 20–35 cm., while that for single induction shocks was 15–25 cm.

The strongest reflex contraction was in most cases obtained at a stimulation-frequency of 40–60 per second. In fig. 1 it is seen that the stimulation-frequency of 59 per second is optimal; the reflex reactions given at quicker or slower rates than this are less powerful as compared with that given at the optimal rate of stimulation. The optimal frequency-rate of stimulation is found to be the same if it is tested in the reverse direction, beginning from the highest rate, and gradually decreasing to the lowest.

It must be remembered that the power of reflex reaction diminishes progressively in a preparation which is used for a prolonged experiment. This is due mainly to the impairment of the central nervous system, as shown by the gradual subsidence of reflex excitability. This change does not depend on any damage to the peripheral mechanism,

since direct stimulation of the motor nerve gives an undiminished response, and shifting the electrodes centralwards on the afferent nerve or elicitation of the reflex by other afferent nerves does not notably affect the degree of impairment. Local damage is more pronounced when a smaller afferent nerve is used. Even when the diminution of reflex excitability is marked, the optimal rate usually remains the same. In fig. 1 there is no sign of such change of excitability throughout the experiment.

(2) *Mechanical Reflex Rhythm with varying Frequency of Stimulation.*—Various results have been obtained by earlier workers in regard to the relation between the frequency of rhythmic stimulation of the afferent nerve and that of the impulses sent out from the spinal centre to the motor organ. Some investigators have shown that the central nervous system tends to reproduce an intrinsic rhythm of innervation, *i.e.*, about 20 per second (Kronecker and Stanley Hall and others), or about 10 per second (Horsley and Schäfer and others), irrespective of the rhythm of excitation applied to an afferent nerve or to the central nervous system itself. Von Limbeck (12) has, however, found that both in warm-blooded and cold-blooded animals, on artificially stimulating the brain or spinal cord by induction currents, the number of muscular vibrations follows the rhythm of stimulation within wide limits. In the frog and toad the contraction of the gastrocnemius muscle, evoked directly by excitation of the spinal cord, or reflexly by stimulation of the sciatic nerve at a frequency-rate of 13 per second, shows the same rhythm as that of stimulation. He notes besides that, at slower rates of excitation, the mechanical vibrations are double the frequency-rate of stimulation, both make and break shocks taking effect. By a more delicate "resonance method" it has been recently shown by Dreyer and Sherrington (5) that the myograph of the reflex contraction in cats exhibits a mechanical rhythm synchronous with the stimulation at rates up to, and even beyond, 55 a second.

In order to re-examine this point in frogs, a myograph recorder, whose vibration-frequency was 30 per second, was employed. The torsion key was placed upon another table, so that the direct mechanical influence of the vibration of this instrument on the recording lever might be avoided. By this resonance method, the reflex myograph of the semitendinosus evoked by stimulating an afferent nerve shows in the majority of cases more or less clear mechanical tremors synchronous with the frequency of stimulation, whether the rate is 15, 20, or 30 per second (figs. 1 and 2). Further increase of frequency of stimulation up to 40 per second is sometimes followed by the same rhythm of reflex contraction. The reflex centre discharge appears to follow the successive volleys of centripetal impulses

at the same rate as those evoked in and transmitted to it by the afferent nerve. The above results in frogs are therefore in agreement with those latest observations referred to above, and are confirmed by investigations made with the string galvanometer (1, 6, 10).

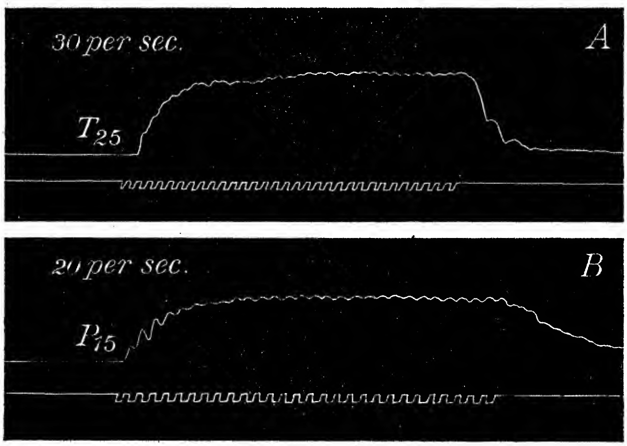

FIG. 2.—Semitendinosus reflex-preparation of spinal frog. The mechanical vibration of muscle synchronous with stimulation frequency. A = tibial nerve; B = peroneal nerve; Number = distance between coils.

When the rate of excitation is low, *e.g.*, 20–30 per second, I have frequently failed to show the synchronism of reflex response with that of the exciting stimuli, though this is clearly evident in the direct tetanus produced by stimulating the motor nerve to the muscle. This is often the case when the excitation at low frequency gives a comparatively high reflex contraction, and in some preparations where the reflex reaction is irregular. The synchronism between the frequency of stimulation of a skin spot of the hind limb and the rhythm of the resulting reflex reaction is soon abolished owing to the irregularity of the reflex response.

(3) *The Course of Reflex Contraction Produced at various Stimulation-Frequencies.*—The course of reflex tetanus is both irregular and variable, at whatever frequency and intensity of excitation it is evoked, as compared with that of direct muscular tetanus. Nevertheless, in typical records some relation between the course of reflex tetanus and the rate of stimulation-frequency which produces it, is usually observed.

With low frequency of stimulation (below 30 per second) it is noted that the reflex contraction, after rapidly attaining its maximum, tends to persist. Often one or two minutes' excitation does not reduce the average height of reaction, though irregular undulations may be seen in the course

of the reflex tracing. The spinal centre excited reflexly at this rate does not appear to be easily fatigued, especially since the contraction is not maximal and time is allowed for recovery during the intervals between stimuli.

At a moderate rate of stimulation (40–60 per second), the typical myogram has a smoother and less undulating form (figs. 1 and 4, D). It attains its maximal height rapidly, and maintains it as a smooth plateau so long as the stimulation continues. If the excitation is prolonged beyond a certain duration the height of the reflex contraction gradually decreases.

At rapid frequency rates the reflex myogram is again irregular. The initial contraction subsides rapidly, especially if the intensity of the stimuli is high (fig. 1). This phenomenon recalls the so-called "initial twitch," which was first described by Bernstein (2) in direct tetanus produced by induction shocks of rapid frequency. The similar "initial reflex tetanus" was noted by Fröhlich (8). At the optimal intensity of stimulation for this high rate the myogram is often quite regular, though fatigue easily occurs. In general, a smooth and regular course of reflex response is associated with a powerful contraction.

The results of my experiments are concordant with those obtained by the study of the action current waves of muscles in reflex reaction, in that the central reflex discharge is optimal, when the spinal reflex centre receives impulses from an afferent nerve at the optimal rate. Though the muscular electrical waves in the reflex tetanus are synchronous with the stimulation rhythm up to 100 per second, in summer frogs (Hoffmann (10), Beritoff (1)), the rhythm at which the reflex centre tends to react may be about fifty per second, and the reflex response at this rate is fairly regular and powerful, as judged by the amplitude of deflection of the galvanometer string (Hoffmann (10)). In my experiments, the optimal rate of stimulation, which averages about fifty per second, gives a smooth and powerful reflex response. The irregularity and diminished height of contraction at frequency rates of stimulation higher than the optimal are in accordance with the observation that the muscular action current waves in reflex responses at rapid frequency present irregularity and rapidly diminishing rhythm.

II. *The Influence of Strength of Stimulation upon the Reflex Reaction.*

The reflex contraction elicited by faradisation at or little above the threshold value is inconstant in regard to the height and progress of contraction. The threshold value itself is continually altering, even in good preparations, though within small limits. When, however, the stimulation is strengthened to a certain intensity, the reflex reaction becomes constant in

height and course. A definite relationship exists between the intensity at different frequency-rates and the extent of the reflex reaction obtained.

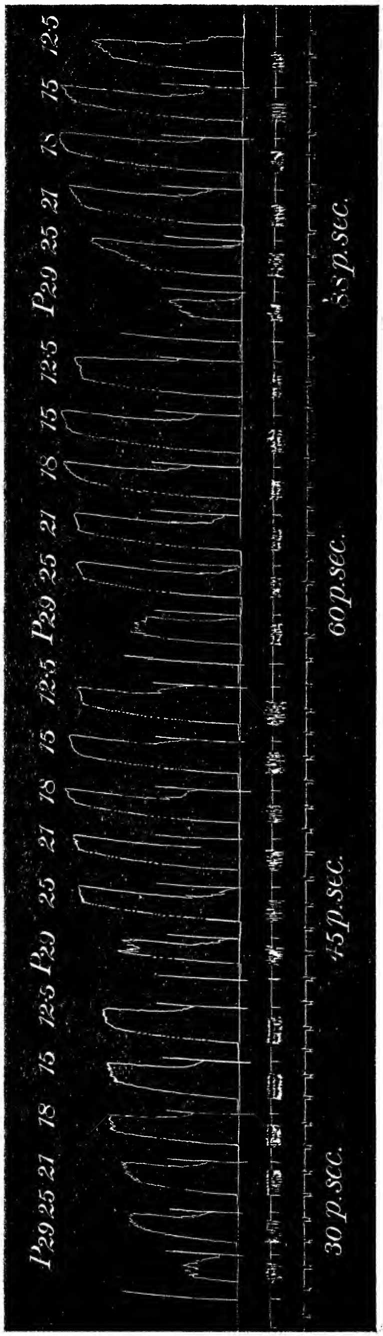

Fig. 3.—Semitendinosus reflex preparation of spinal frog. Groups of responses with frequencies of 30, 45, 60, and 88 per second. The numbers above each response = distance between coils. Time in seconds.

Two methods were adopted of examining this point. In both, several series of reflex responses were recorded. In the first, the frequency was fixed for each series, and the intensity varied within it. In the second, the intensity was fixed for each series, and the rate of stimulation varied.

(1) *Frequency Fixed, Intensity Varied.*—With low rates (under thirty per second), the reflex reaction increases with the intensity of stimulation, at first quickly and then more slowly. Sometimes an intensity is reached, after which no further increase of contraction can be elicited by further increase in the intensity of stimulation. At higher frequency-rates (more than sixty per second), the reflex contraction increases rapidly with the strength of stimulation to a maximum, and from this point decreases with each increment of stimulation. An optimal intensity of stimulation therefore exists at this frequency-rate. Between these two extremes there is a critical value of the frequency-rate, at which the height of contraction remains almost constant after quickly attaining its maximum, in spite of steady increase of intensity of stimulation. In other words, the strength of the reflex reaction under this optimal rate of frequency is independent, within wide limits, of the strength of the stimulation

(figs. 3 and 5). The critical value of stimulation-frequency often coincides with the optimal rate, and is approximately constant in any preparation, as long as this remains in good condition without serious change of reflex excitability.

(2) *Intensity Fixed, Frequency Varied.*—In this method the optimal rate of stimulation in each series is found. If the amplitude of any reflex reaction in one series is compared with the corresponding one in a series obtained at lower intensity, it is found that the reflex response at low frequency is less powerful with low intensity than with higher, while the opposite is the case with greater frequency of stimulation. There has been a shift of the optimal frequency from a lower value at higher intensity to a higher one at lower intensity. Therefore, if the optimal intensity of stimulation for the highest frequency employed has been found, and a series of reflex reactions is registered at this intensity and at progressively increasing rates, the amplitude of reflex response is not infrequently found to increase to the maximum with increase of stimulation-frequency.

The presence of an optimal intensity of stimulation is not limited to very rapid frequency-rates. With moderate frequency it is usually observed, that by increase of intensity beyond a certain value, the reflex reaction thus evoked is less powerful, though the decrease is not so obvious as at higher frequencies (fig. 3). This phenomenon is more marked in some preparations, particularly in those which are impaired by prolonged experiment or are observed during the cold season. Even with a frequency as low as thirty per second, an optimum value may sometimes be obtained if a wide range of intensity is employed. Generally, the higher the stimulation-frequency, the more evident is the existence of an optimal intensity. I have several times observed that the optimal frequency is lower in winter frogs than in summer; in such cases the optimal intensity is more marked with comparatively lower frequencies.

In speaking of an optimal rate of stimulation, it might seem more reasonable to limit the term to the value obtained at the optimal intensity. The latter value is, however, dependent upon the frequency at which it is elicited. Sometimes the reflex response obtained at the optimal intensity at rapid frequencies is equal to, or even greater than, that obtained at the optimal frequency (fig. 3). The contraction has in these cases a smooth and regular course. This optimal intensity of stimulation is evidently of central origin, since a series of direct neuromyal tetani, produced with progressively increasing intensity of faradisation, presents no evidence of the existence of optimal values, except at frequency-rates considerably more rapid than those which exhibit it in the reflex observations (see later). The degree of

peripheral tetanus produced increases with the strength of stimulation, until the maximum is obtained for any given frequency-rate, and beyond this point there is no decline, but an unvarying response is given with progressively increasing stimuli.

The experimental results here described concerning the influence of intensity and frequency of stimulation upon the reflex response are in accord with the observations of Wedensky (19), Hoffmann (9) and others, on peripheral tetanus, usually spoken of as "Wedensky's phenomena." When the muscle is tetanised from its motor nerve with strong induction shocks of considerable frequency it relaxes more or less quickly. If the stimuli are then weakened to a certain extent the muscle again falls into a powerful tetanus (Optimum der Reizstärke). If, however, they are again strengthened it enters into its former relaxed condition (Pessimum der Reizstärke). A similar result is obtained by altering the frequency at high intensity of stimulation. For the fresh muscle of the frog, the optimal frequency of stimulation, at which the highest contraction is obtainable in the shortest time, is about 100 stimuli per second (60–150). When lower frequency (about twenty per second) or higher frequency of stimulation (over 260 per second) is used the muscle never attains its maximal shortening in any phase of tetanus. If the preparation is in an unfavourable condition as a result of fatigue or poisoning by ether or curare the optimal frequency of stimulation is lower and the optimal intensity is obtained at lower frequency. On comparing the results in peripheral and reflex tetanus under normal conditions, the most noteworthy difference is that in the latter the optimal frequency of stimulation is lower than in the former; the latter, therefore, only corresponds to the former when the preparation is under unfavourable condition. Another striking difference, though not a constant one, is seen to exist between direct and reflex tetanus produced by pessimal intensity of stimulation. The muscle, in the latter case, often enters into a more exaggerated contraction or goes into contraction (if this has not been present during its course) when the stimulation is discontinued. The after-discharge which appears in any reflex contraction does not usually surpass the height of tetanus obtainable during the application of stimulation, except when the reflex is produced by pessimal intensity of stimulus.

These observations on optimal intensity have a superficial resemblance to those of Sherrington and Sowton (17) on the tonic contraction of the knee-extensor which was augmented by weak stimulation and inhibited by stimuli of stronger intensity. A similar change of response to stimuli of altered intensity is exhibited by the opening muscle of the claw of the crayfish (3, 7, 13, 15).

III. *The Comparison of Reflex Tetanus with Peripheral Tetanus at varying Rates of Stimulation.*

To examine this point, the afferent nerve was faradised at the optimal intensity for a given frequency-rate, and the resulting reflex tetanus registered by a spring myograph. For comparison, a direct tetanus was produced by faradisation of the motor nerve under the same condition of stimulation.

The differences in the observations of the previous workers (Marey, Bohr, Bernstein, Kohnstamm, Wedensky, Hoffmann and others) on myal and neuromyal tetanus produced at varying rates and intensities of stimulation are to be explained by the different conditions under which the problem was studied. Some observations necessary for the present inquiry in this respect were repeated with the method which I have used in these experiments.

The extent of direct tetanus with increasing intensity of stimulation of a given frequency-rate only increases up to a certain point, and thereafter shows no further increase. The optimal intensity of stimulation for reflex excitation is usually somewhat higher than the maximal intensity for direct tetanus. A series of records of neuromyal tetanus, which was made with progressively rising frequency-rate of stimulation of maximal strength, and in which the stimulation was continued until the maximal contraction was attained in each case, shows no significant increase in the power of contraction with increase of the frequency-rate of stimulation beyond about 50 per second. From these observations it appears that the maximal tetanus produced by the maximal intensity of stimulation for a given frequency greater than 50 per second can be regarded as the maximal contraction of the muscle.

On comparing reflex tetanus with direct tetanus produced at low frequency-rates of stimulation (under 30 per second) with the same intensity, the former is usually more abrupt and more powerful than the latter in the early period of contraction. This fact shows that the discharge of impulses from the reflex centre is at a higher rate than that of stimulation applied to the afferent nerve, and further suggests that some of the component shocks used as stimuli evoke from the spinal reflex centre repetitive volleys of motor impulses, since it has already been shown that at low frequency-rates the rhythm of repetition of volley discharges from the centre is synchronous with the rate of stimulation. A similar conclusion was drawn by the comparison of reflex contraction produced by a single strong momentary stimulus applied to the afferent nerve with a direct twitch produced by

a like stimulus (5, 16). If excitation is applied longer at this rate the direct tetanus increases in power, while the reflex tetanus decreases, or slowly increases, only to decrease later, so that the former always surpasses the latter in the maximal power produced. This indicates that fatigue is more easily produced in the central than in the peripheral mechanism.

At the optimal rate of stimulation the reflex contraction is often nearly as powerful and abrupt in the first period of tetanus as the direct one (fig. 4). If the excitation is prolonged, the direct tetanus soon attains the maximum, which is maintained for a long time, while the reflex tetanus diminishes in height. The difference of the maximal contraction in both cases is often extremely slight in good preparations. This observation suggests that the spinal centre is a physiological unity, any one afferent nerve being connected with all the motor neurons of the reflex arc, since there is some evidence that each component shock of faradisation applied to an afferent nerve at the rate of more than 50 per sec. is followed by only one motor impulse, not by a group of impulses (1). The result more usually obtained, that reflex tetanus falls more or less short of direct tetanus, is partly due to the fact that the reflex centre is more easily fatigued than the muscle itself. It must further be remembered that it is often difficult to make out exactly the optimal intensity. At rapid frequency of stimulation the direct is usually more powerful than the reflex tetanus.

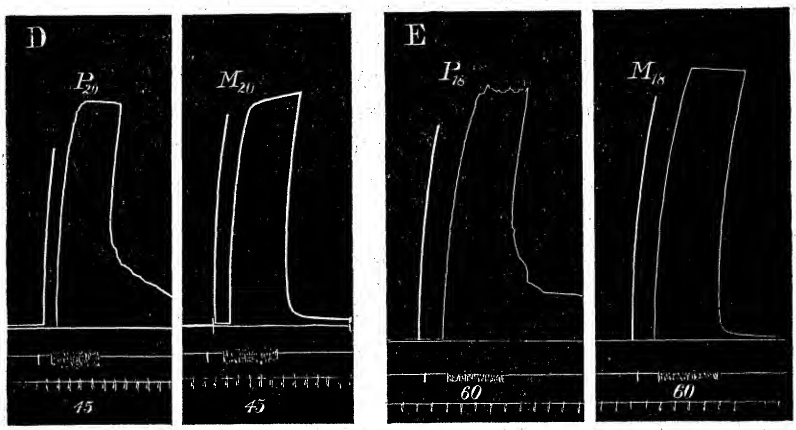

Fig. 4.—Semitendinosus preparation. Comparison of reflex (P) with maximal direct tetanus (M). D = frequency 45 per sec. and 20 c.m.; E = 60 per sec. and 18 cm.; P = peroneal nerve stimulation. M = sciatic roots stimulation. Time in sec.

The afferent nerves hitherto used were nerve trunks, such as the tibialis, peroneus, or sciatic. The extent of the reflex contraction produced by stimulating these afferent nerve trunks shows only small differences. A stronger

reaction is not necessarily obtained by stimulating more afferent nerve fibres. The comparison of the maximal reflex reaction produced by exciting either a very slender afferent nerve or the skin of toes with that evoked by faradising a nerve trunk has an important bearing on the question of the physiological unity of the spinal reflex centre.

The ramus cutaneus medius was isolated with a tiny piece of the skin which it innervates. The threshold value for this nerve is usually higher than that of the peroneal trunk, a fact which may be related to the ease with which it is injured. Nevertheless, sufficiently strong faradisation of the nerve when it is freshly prepared and has a comparatively low threshold value often produces as powerful a reflex contraction as does that of the peroneal. The extent of the reflex reaction evoked by a small nerve appears to depend more upon the intensity than upon the rate of stimulation. The extent of reflex reaction can be graded with graded strength of excitation. Sometimes the skin of toes was excited by applying a pair of electrodes two or three millimetres apart. The reflex contraction thus produced often attains the intensity of that evoked by stimulating a nerve trunk (fig. 5). The course of the reflex response elicited by a stimulation of a small afferent nerve or a skin-spot is irregular.

The fact that the reflex contraction produced by a stimulation of a small

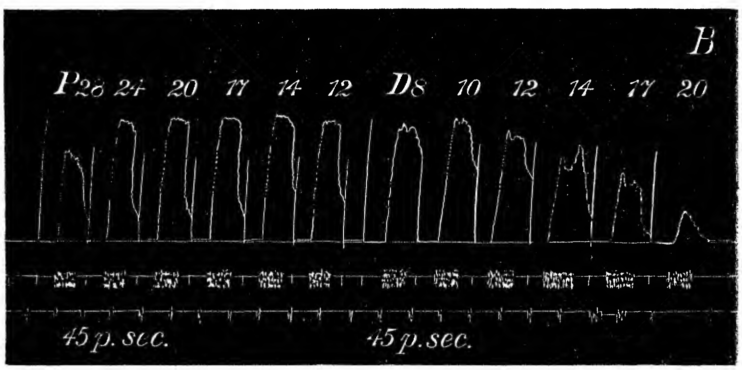

FIG. 5.—Semitendinosus reflex preparation. Responses at same frequency of stimulation (45 per second) with varying intensity. P = peroneal nerve; D = skin (2nd toe) stimulation. Numbers = distance between coils. Time in sec.

afferent nerve or of a circumscribed skin point is of the same extent as that elicited from a nerve trunk and sometimes nearly equal to the maximal direct tetanus suggests strongly the physiological unity of the reflex centre, any afferent nerve, even a small skin nerve, being connected with the whole motor reflex centre.

Conclusions.—(1) There is an optimal intensity of stimulation at rapid

frequency-rates, *i.e.*, more than 60 per sec., for the reflex power produced in the semitendinosus muscle of the spinal frog, if an ipsilateral afferent nerve trunk is stimulated. At moderate frequency-rates (50 per second on average) the reflex result depends but little upon the intensity of excitation. At low rates (under 30 per second) the reflex response increases with the strength of stimulation, at first quickly and then slowly. The maximum, when attained, is maintained for further increments of stimulation; no optimum is usually seen.

(2) Similarly there is an optimal rate of stimulation for any given intensity which is usually about 50 per second. At the optimal intensity of stimulation for a rapid frequency the reflex power at this frequency may often be equal to or even somewhat greater than that produced at the optimal rate.

(3) The reflex myogram obtained by the resonance method exhibits mechanical vibrations synchronous with the frequency-rate of stimulation when this is under 30 per second. The spinal reflex centre therefore follows at the same rate the rhythm of successive volleys of centripetal impulses.

(4) The reflex tetanus evoked by faradising at sufficient intensity an afferent nerve at rates less than 30 per second, is more abrupt and more powerful in the first period of contraction than the direct tetanus produced under the same condition of excitation, though the latter always surpasses the former when the stimulation is prolonged. Therefore some of the component shocks used as stimuli produce a repetitive series of motor impulses from the reflex centre.

(5) The reflex contraction evoked at the optimal rate of excitation is often nearly as powerful as the direct one obtained by similar stimulation, especially in the first period of contraction.

(6) The faradisation of a very small afferent nerve-branch (ramus cutaneus medius) or of a circumscribed skin spot often produces as powerful a reflex contraction as that obtained by stimulation of a nerve trunk at the same frequency. The results obtained in (5) and (6) suggest that the motor reflex centre is a physiological unity; any afferent nerve, even a small one, being connected with all the motor neurons of a reflex arc.

I am greatly indebted to Prof. C. S. Sherrington for continuous suggestions and advice during the progress of these experiments, and for permission to utilise his instruments. I take also this opportunity in thanking Dr. C. H. Kellaway for kind assistance in expressing the results in the text.

REFERENCES.

(1) Beritoff, J. S., 'Zeitschr. Biol.,' vol. 62, p. 126 (1913); vol. 64, p. 161 (1914).
(2) Bernstein, J., 'Untersuchungen üb. d. Erregungsvorgang im Nerven u. Muskelsysteme,' Heidelberg, 1871, p. 100.
(3) Biedermann, W., 'Sitzungsber. d. Kaiserl. Akad. Wien.,' vol. 95, III, p. 1 (1887).
(4) Camis, M., 'Journ. Physiol.,' vol. 39, p. 228 (1909).
(5) Dreyer, N. B., and C. S. Sherrington, 'Roy. Soc. Proc.,' B, vol. 90, p. 270 (1918).
(6) Foà, C., 'Zeitschr. allgem. Physiol.,' vol. 9, p. 55 (1909); 'Centralblatt Physiol.,' vol. 24, p. 792.
(7) Fröhlich, F. W., 'Zeitschr. allgem. Physiol.,' vol. 7, p. 393 (1908).
(8) Fröhlich, F. W., 'Zeitschr. allgem. Physiol.,' vol. 9, p. 55 (1909).
(9) Hoffmann, F. B., 'Pflüger's Archiv,' vol. 93, p. 186 (1903); vol. 95, p. 484 (1903); vol. 103, p. 291 (1904).
(10) Hoffmann, P., 'Arch. Physiol.,' 1911, Suppl., p. 286.
(11) Kronecker, H., and Nicolaides, 'Arch. Physiol.,' 1880, p. 437.
(12) Limbeck, R., 'Arch. Exper. Pathol. Pharm.,' vol. 25, p. 171 (1888).
(13) Luchsinger, B., 'Pflüger's Archiv,' vol. 28, p. 60 (1882).
(14) Mattaei, R., 'Zeitschr. allgem. Physiol.,' vol. 18, p. 281 (1919).
(15) Richet, C., 'Physiol. des Muscles et des Nerfs,' Paris, 1882, p. 74.
(16) Sassa, K., and C. S. Sherrington, 'Roy. Soc. Proc.,' B, vol. 92, p. 110 (1921).
(17) Sherrington, C. S., and S. C. M. Sowton, 'Roy. Soc. Proc.,' B, vol. 83, p. 435 (1911).
(18) Stirling, W., 'Ber. d. Sächs. Gesellsch. Wissensch. Leipzig, Math.-Phys. Kl.,' vol. 26, p. 372 (1874).
(19) Wedensky, cited in F. B. Hoffmann's paper.

On the Effects of Constant Galvanic Currents upon the Mammalian Nerve-Muscle and Reflex Preparations.

By KANSHI SASSA, M.D., Tokio.

(Communicated by C. S. Sherrington, Pres. R.S. Received July 8, 1921.)

(From the Physiological Laboratory, Museum, Oxford.)

My experiments were to study the reflex effects resulting from stimulation by constant galvanic currents applied to an afferent nerve of the hind limb. The main points of enquiry have been: (1) the relation between reflex excitation and inhibition of the decerebrate tonus of the vasto-crureus; (2) whether the "excitation formula" (Pflüger's law) holds good in mammalian afferent nerves; and (3) whether there is continuous excitation during the passage of the current through an afferent nerve.

The reflex effects thus produced in the extensor muscle are complex and various, and are difficult to analyse without accurate knowledge of the results